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Acute Kidney Injury in Neonates: A Single-Center Experience

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Abstract:

Background: Neonatal intensive care unit infants frequently experience acute kidney damage. Estimates of the prevalence of acute kidney vary depending on the definitions used. In Iraq, studies addressing the prevalence and risk factors of acute kidney injury in this age group are scarce, none of which has implicated the KDIGO diagnostic and staging criteria.

Objectives: To describe the prevalence, demographics, risk factors, etiology, and staging of acute kidney injury using KDIGO criteria in the Neonatal intensive care unit and correlate these findings with patient outcomes.

Methods: A retrospective study was conducted in the Neonatal Intensive Care Unit/ CWTH/ Medical City Complex/ Baghdad during the period from the 1st of August 2019 to the 15th of January 2020. All neonates diagnosed with acute kidney injury according to KDIGO –classification 2012 and admitted to the neonatal intensive care unit were included in this study. Demographics, clinical staging, and investigations were retrieved from patients' notes.

Results: The prevalence of acute kidney damage was 7.2%. The mean gestational age of the patients was 36.8 ± 2.9 weeks, 58% of them were full-term, with a male-to-female ratio of 1.40:1. Stage I patients represented 35.1%, 43.2% were stage 2, and 21.6% had severe stage 3. Acute kidney injury-related mortality was 35.1%. The term female sex, high birth weight, and age younger than seven days at diagnosis predicted a bad prognosis. Vaginally delivered, stage III acute kidney injury-KDIGO, and peritoneal dialysis patients had the worst outcomes. Asphyxia was a major cause of acute kidney injury (P=0.001). High blood urea (P=0.01), low PH (P=0.009), low HCO3 (P=0.001), low WBC count (P=0.001), and low platelet count (0.001) were associated with unfavorable outcomes.

Conclusions: The prevalence of acute kidney injury, according to KIDGO diagnostic and staging criteria, is 7.1%. Asphyxia, female gender, and vaginal deliveries are variables associated with poor prognosis in addition to advanced illness stage and laboratory indicators.

Keywords: Acute kidney disease, KDIGO criteria, Neonatal intensive care unit, neonates, prevalence.

Introduction

Neonatal intensive care unit (NICU) infants frequently experience acute kidney damage, which is linked to higher rates of death and morbidity and a higher risk of developing chronic renal disease (AKI)(1). AKI can be defined as a rapid decline in the kidney's ability to maintain homeostasis of water and electrolytes associated with a reduction of the glomerular filtration rate (2).

Studies have revealed that AKI occurs in 18% of very-low-birth-weight newborns, 52% of infants who underwent surgery for congenital heart disease, and 9% and 56% of infants with mild and severe birth asphyxia, respectively, however, estimates of the incidence of AKI vary depending on the definitions employed (3).

The use of the neonatal Kidney Disease Improving Global Outcomes (KDIGO) of neonatal AKI in 2012 has resulted in a dramatic increase in our knowledge of the epidemiology of neonatal AKI over the past decade. The most up-to-date classification system, the modified KDIGO consensus definition, is a synthesis of the RIFLE, AKIN, and pRIFLE (4).

The AWAKEN trial, the largest of its kind to date, reported an overall incidence of AKI within NICU to be 30% (5). In Iraq, studies addressing the prevalence and risk factors of AKI in this age group are scarce, none of which has implicated the KDIGO diagnostic and staging criteria. This study aimed to describe the prevalence, demographic characteristics, risk factors, etiology, and staging of AKI using the KDIGO criteria in our NICU and to correlate these findings with the patient's outcome.

Methods

This was a retrospective study conducted in the Neonatal Intensive Care Unit (NICU) / Children Welfare Teaching Hospital (CWTH) / Medical City Complex / Baghdad during the period from 1st of August, 2019 to 15th of January 2020. The study

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was approved by scientific and ethical committees of the Arab Board -Scientific Council and CWTH.

All neonates diagnosed with AKI according to KDIGO –classification 2012 and admitted to NICU / CWTH were included in this study. Patients were excluded if death occured within the first 24 hours after admission to NICU, if they had a known maternal renal disease, or if parents decided to leave the hospital on their responsibility. Gestational age (GA) was classified as the following: early preterm < 34 weeks GA, late preterm neonates 34+0 -36+6 weeks GA, term neonate 37 + 0 – 41+6 weeks GA, post-term neonate > 42 weeks GA (6). Neonatal birth weight (BW) was classified as the following: Low birth weight <2500g, normal birth weight from 2500g – 3999g; high birth weight 4000g- 4500g (6).

Diagnosis of AKI in neonate was made by the presence of least one of the following: High serum creatinine >1.5 mg /dl, increasing in serum creatinine at least (0.3 mg /dl / 24 hrs., or 1.5 times from the lowest serum creatinine level) or oliguria urine output (<1ml /kg/hr. for 24 hours) or all of them (7). Staging of AKI according to the (Kidney Disease / Improving Global Outcomes) KDIGO classification 2012 (7).

Biochemical and hematological investigations were available for all included patients. Values were according to normal range references for age used by CWTH laboratory as follows: Blood urea (normal range up to 45 mg /dl), Blood gas analysis values as the following: (serum Ph 7.35- 7.45 and HCO3 22-26 mEq/L), serum potassium 3.5-5 mmol/L, serum calcium 8 – 10.8 mg/dl, serum sodium 130-145 mmol/L, platelets counts 150x10 ^{9} / L, Hb 14- 20 g /dl and WBC 5000- 20000 x10^{9} /L.

Patients' treatments and outcomes were retrieved from their records whether discharged after restoring normal (or there was mildly diminished) renal function with follow up, normal urine output or normal laboratory investigation result) or dead.

Statistical analysis

All neonatal data were entered using computerized statistical software; Statistical Package for Social Sciences (SPSS) version 22 was used. Descriptive statistics are presented as (mean ± standard deviation) and frequencies as percentages. Multiple contingency tables were conducted and appropriate statistical tests were performed, Chi-Squared test was used for categorical variables (Fishers exact test was used when the expected variable was less than 20% of the total variable). In all statistical analyses, the level of significance (p-value) was set at ≤ 0.05.

Results

During the study period, a total of 1031 neonates were admitted to NICU, and 74 (7.2%) neonates were diagnosed with acute kidney injury (AKI).

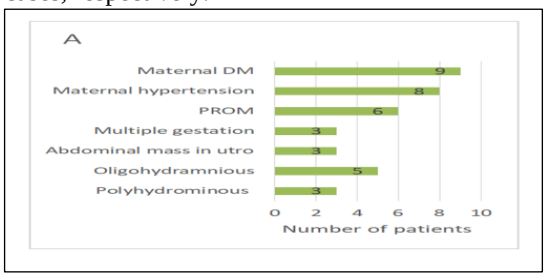
The demographics and characteristics of AKI patients are summarized in Table 1. Patients had a mean gestational age of 36.8 ± 2.9 weeks ; 43 (58.1%) were full-term, with a slight male predominance; the male-to-female ratio was 1.40:1. Mean newborn age at diagnosis was 7.4 (6.1) days, with 34 (45.9%) diagnosed between 1 and 3 days of age. Their mean birth weight was (2.9 kg ±0.8), with 29.7% having a low birth weight and 6.8% having a high BW. In more than half of the cases 44 (59.5%), surgical delivery was documented.

Table 1 Demographics and clinical characteristics of AKI patients

Variable	No.	%
Gestational age Mean ±SD (36.8±2.9 weeks)		
Early preterm	10	13.5
Late preterm	21	28.4
Term	43	58.1
Gender		
Male	44	59.5
Female	30	40.5
Age when AKI diagnosed Mean ±SD (7.4±6.1 days)		
1-3 days	34	45.9
4-7 days	14	18.9
>7 days	26	35.1
Birth weight Mean ±SD (2.9±0.8 Kg)		
Low birth WT	22	29.7
Normal birth WT	47	63.5
High birth WT	5	6.8
Mode of delivery		
vaginal delivery	30	40.5
Cesarean section	44	59.5
AKI stage at time of diagnosis		
Stage 1	26	35.1
Stage 2	32	43.2
Stage 3	16	21.6
Patients Outcome		
Discharged	48	64.9
Dead	26	35.1
Dead	26	35.1
Total	74	100.0

Clinical examination and laboratory analysis revealed that 35.1% of the patients were in stage 1, 43.2% were in stage 2, and 21.6% were in advanced stage 3.

As depicted in Figure 1A, maternal and prenatal risk factors for AKI were positive in 37 (50%) of patients with maternal DM (24.1%), maternal hypertension (21.6%), and premature rupture of membranes (16%) being the most prevalent. Figure 1B shows the various causes of AKI; sepsis and prenatal asphyxia accounted for 40.5% and 23% of AKI cases, respectively.



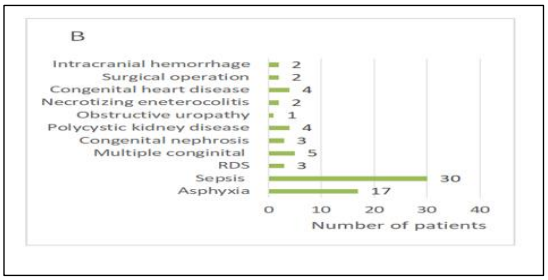


Figure 1 Risk factors and etiology of AKI patients. Abbreviation: PROM, premature rupture of membrane; RDS, respiratory distress syndrome.

The mortality rate for patients with AKI was 35.1%. Term, female sex, high birth weight, and age less than seven days at diagnosis were significantly associated with a poor prognosis. In addition, individuals who were vaginally delivered had a severe illness and required peritoneal dialysis and had considerably worse outcomes, as seen in Table 2.

Table 2 Association between AKI patient's characteristics and outcome

Variable	Outcome				*P value*
	Discharge		Dead		
	No	%	No	%	
Gestational age of groups					0.04
Early preterm	10	20.8	0	-	
Late preterm	12	25.0	9	34.6	
Term	26	54.2	17	65.4	
Gender					0.001*
Male	35	72.9	9	34.6	
Female	13	27.1	17	65.4	
Age on AKI diagnosis					0.001*
1-3 days	17	35.4	17	65.4	
4-7 days	7	14.6	7	26.9	
>7 days	24	50.0	2	7.7	
Birth weight Mean ±SD(2.9±0.8 Kg)					0.002
Low	18	37.5	4	15.4	
Normal	30	62.5	17	65.4	
High	0	-	5	19.2	
Mode of Delivery					<0.001
Vaginal delivery	11	22.9	19	73.1	
Caesarian Delivery	37	77.1	7	26.9	
Maternal & antenatal risk factor					0.3
Neonates& maternal	22	45.8	15	57.7	
Neonatal	26	54.2	11	42.3	
AKI stage at time of diagnosis					0.004
Stage 1	21	43.8	5	19.2	
Stage 2	22	45.8	10	38.5	
Stage 3	5	10.4	11	42.3	
Dialysis required					<0.001
No	47	97.9	10	38.5	
Potential dialysis	1	2.1	16	61.5	

There was no significant association between patient outcome and maternal and prenatal risk factors, according to Table 2 and Figure 2A. Poor patient outcome was substantially linked with neonatal asphyxia as a cause of AKI (P<0.001), as shown in Figure 2

A significant association was observed between high blood urea (p=0.01), low PH (P=0.009), low HCO3 (p<0.001), low WBC count (P<0.001), low platelet count (<0.001), and worse outcome in AKI patients. No significant association was observed between K+, serum Ca++ and serum Na++ levels and poor outcomes, Table 3.

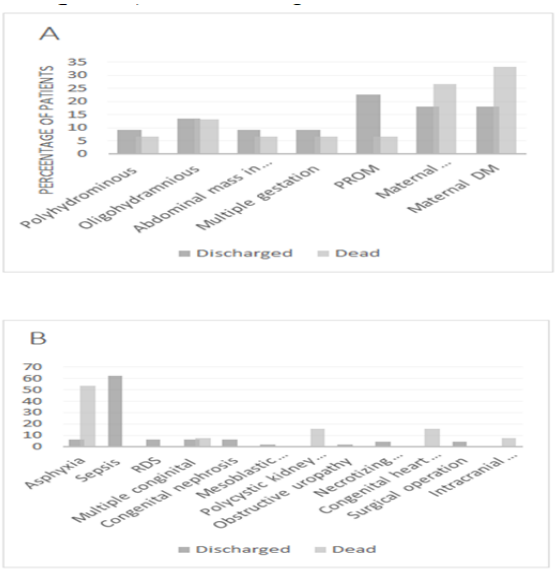


Figure 2 Outcome of AKI Patients according to A) risk factors and, B) Etiology. Abbreviation: PROM,

Table 3 Association between laboratory findings and AKI patients` outcome

Variable	Outcome				*P*
	Discharged		Dead		
	No.	%	No.	%	
Blood urea Mean ±SD (77.5±43.4 mg/dl)					0.01
Normal	10	20.8	0	-	
High	38	79.2	26	100.0	
Blood PH Mean ±SD (7.2±0.18)					0.009
Low	34	70.8			
Normal	11	22.9			
High	3	6.3			
HCO3 Mean ±SD (13±6.7 mEq/L)					<0.001
Low	27	56.3	26	100.0	
Normal	14	29.2	0	-	
High	7	14.6	0	-	
Serum K^+ Mean ±SD (6.3±5.5 mEq/L)					0.06
Low	7	14.6	0	-	
Normal	28	58.3	14	53.8	
High	13	27.1	12	46.2	
Serum Ca^{++} Mean ±SD (8.2±1.6mEq/L)					0.06
Low	6	12.5	5	19.2	
Normal	33	68.8	21	80.8	
High	9	18.8	0	-	
Serum Na^+ Mean ±SD (130.6±8.3mEq/L)					0.07
Low	25	52.1	9	34.6	
Normal	23	47.9	15	57.7	
High	0	-	2	7.7	
Hb Mean ±SD (13.8±33 g/dl)					
Normal	31	64.6	18	69.2	
Anemic	17	35.4	8	30.8	
WBC count Mean ±SD (16.4±7.2X10^9)					<0.001
Low	0	-	5	19.2	
Normal	18	37.5	8	30.8	
High	30	62.5	13	50.0	
Platelets count Mean ±SD (270.7±175.8X10^9)					<0.001
Low	21	43.8	24	92.3	
Normal	19	39.6	2	7.7	

Discussion

Acute kidney injury (AKI) is a devastating illness that commonly affects neonates; however, the worldwide incidence of AKI remains unknown. Modified KDIGO definition in 2012 has been implicated in harmonizing the diagnosis and stage AKI in neonates (4). To our knowledge, this is the first Iraqi study that uses the modified KDIGO definition to describe the prevalence and mortality of AKI in one of the largest NICU centers in Iraq.

The prevalence of AKI in neonates is relatively underestimated. A recent large multicenter study including 24 NICU centers and 2022 neonates, reported an AKI prevalence of 30% (5). Earlier studies reported a 21.8% prevalence in full-term neonates according to nRIFLE criteria (8). In the current study, AKI prevalence was 7.17% which is much higher than a previous study from the same center in 2009 which reported a prevalence as low as 2% (9). This is, however, lower than regional figures. A single-center Saudi study reported a 56% incidence of AKI in NICU admission according to modified neonatal KDIGO stages (10) while an Egyptian study recorded a 10.0% prevalence in 2015 (11).

As a newborn's kidneys are more sensitive to hypoperfusion and have a poor glomerular filtration rate, The significance and complexities of AKI are amplified in newborn patients (4). In the current study, about two-thirds of the included cases were categorized as stage II and III while stage I represented only (35.1%). By contrast, another study has shown a higher frequency of Stage I disease up to 60% (8) which may be related to the smaller number of AKI cases in the cohort which was limited to 35/160. The Death (case fatality) rate in this study was 35.7% which is close to a regional study by Momtaz et al (12) who reported a mortality rate of 36.7% in an Iranian NICU center whereas El-Badawy et (13) and Shalaby et al (10) reported different rates ranged between 51% and 28.3% in Egypt and Saudi respectively. While differences in mortality rates across these studies may reflect the quality of medical services in NICU centers, it may be also related to the risk factors and underlying pathology as well as study design and inclusion criteria. Among the comorbidities and risk factors that are strongly associated with AKI are sepsis, shock, and birth asphyxia (8). We have shown that sepsis was significantly associated with AKI mortality. We also found that full-term newborns had a significantly higher risk of dying from AKI than preterm neonates did (p=0.04) this could be because 58.2% of neonates in this study were full-term, although similar findings were reported by the Indian study conducted by Bansal et al.(14), which found a greater mortality rate in term infants compared to preterm neonates. Additionally, our findings, which are in line with those of earlier research (14), showed both female sex and high birth weight were associated with AKI-related death. The risk of death from AKI was also significantly associated with vaginal delivery. Consistent with our results, a study conducted in the United States by Charlton JR29 et al (15) found that scheduled cesarean section (in comparison to vaginal birth) was related to a 30% decreased probability of early AKI. The current study reported also a significant association between low PH and HCO3 of neonates and death outcome and this may be because these factors are associated with the advanced staging of AKI. Furthermore, we found a significant association between anemia, low platelet, high WBC counts, and AKI-related mortality. Similar findings were reported by other studies (16-18).

Conclusions

The prevalence of AKI according to KIDGO diagnostic and staging criteria is 7.1%. Asphyxia, female sex, and vaginal deliveries are factors associated significantly with poor outcomes in addition to advanced disease stage and associated laboratory indicators.

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Author's contributions

YIS and AAK designed the study; AAK, AKK, and KZA collected the data and drafted the results, AKK drafted the manuscript and all authors revised the manuscript and approved it.

Authors' declaration:

Conflicts of Interest: None.

We confirm that all the Figures and Tables in the manuscript are ours. Authors sign on ethical consideration's approval-Ethical Clearance: The local ethical committee approved the project i**n the NICU of Children Welfare Teaching Hospital according to code number (**ISU-4523 - 16/1/2029**).**

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اصابات الكلى الحادة عند حديثي الولادة: خبرة مركز واحد

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الخلفية: يعاني الرضع في وحدة العناية المركزة لحديثي الولادة في كثير من الأحيان من تلف حاد في الكلى.تختلف تقديرات انتشار القصور الكلوي الحاد اعتمادًا على التعريفات المستخدمة. في العراق ، تعد الدراسات التي تتناول انتشار وعوامل الخطر المرتبطة بمرض تلف الكلى الحاد في هذه الفئة العمرية نادرة ، ولم يشر أي منها إلى معايير التشخيص والمراحل الخاصة بـ KDIGO.
الهدف: وصف عدد ، والتركيبة السكانية ، وعوامل الخطر ، والمسببات ، والتدريج لمرض القصور الكلوي الحاد باستخدام معايير KDIGO في وحدات العناية المركزة لحديثي الولادة وربط هذه النتائج بنتائج المرضى.
الطريقة: تم إجراء دراسة وصفية تحليلية بأثر رجعي في وحدة العناية المركزة لحديثي الولادة/ المستشفى التعليمي لرعاية الأطفال / مجمع مدينة الطب / بغداد خلال الفترة من 1 آب 2019 إلى 15 كانون الثاني 2020. جميع حديثي الولادة الذين تم تشخيص إصابتهم بتلف الكلى الحاد وفقًا لتصنيف KDIGO - تصنيف 2012 و ادخالهم في وحدة العناية المركزة لحديثي الولادة تم تضمينه في هذه الدراسة. تم استحصال المعلومات الديموغرافية والسريرية لمراحل المرض من فايلات المرضى, تم استبعاد المرضى إذا ماتوا في غضون 24 ساعة من دخولهم إلى وحدة العناية المركزة لحديثي الولادة ، أو إذا كان لديهم الام مرض كلوي ، أو إذا غادر االوالدان المستشفى على مسؤوليتهم.
النتائج: كان انتشار القصور الكلوي الحاد 7.1 ٪. كان متوسط عمر الحمل للمرضى 36.8 أسبوعًا ± 2.9. كانت نسبة 58.1٪ من المرضى ذوي مدة حمل مكتملة ، حيث بلغت نسبة الذكور إلى الإناث 1.40 :1. يمثل مرضى المرحلة الأولى 35.1٪ ، 43.2٪ هم المرحلة الثانية ، و 21.6٪ لديهم المرحلة المتقدمة الثالثة. معدل الوفيات المرتبطة بتلف الكلى الحاد كان 35.1٪. اكتمال الحمل ، والجنس الأنثوي ، والوزن المرتفع عند الولادة ، والعمر الذي يقل عمره عن سبعة أيام عند التشخيص تنبأ بالتشخيص السيئ. كان للمرضى الذين تم ولادتهم طبيعية ، والمرحلة الثالثة ، ومرضى غسيل الكلى البريتوني أسوأ النتائج. كان الاختناق سببًا رئيسيًا لـ تلف الكلى الحاد (P= 0.001). ارتبط ارتفاع اليوريا في الدم (p = 0.01) ، وانخفاض PH (p = 0.009) ، وانخفاض HCO3 (P<0.001) ، وانخفاض عدد كرات الدم البيضاء (P<0.001) ، وانخفاض عدد الصفائح الدموية (P<0.001) بنتائج غير جيدة للمرضى.
الاستنتاجات: انتشار تلف الكلى الحاد وفقًا لمعايير KIDGO التشخيصية والتدريجية هو 7.1 ٪. الاختناق والجنس الأنثوي والولادات الطبيعيةهي متغيرات مرتبطة بسوء الحالة بالإضافة إلى مرحلة المرض المتقدمة والمؤشرات المختبرية.
الكلمات المفتاحية : اصابات الكلى الحادة ، وحدة العناية المركزة لحديثي الولادة ، حديثي الولادة ، الانتشار ، معايير KDIGO.